DO NOT ENTER 3/16/05 MAM

AMENDMENTS TO THE CLAIMS

1. *(Currently Amended)* A computer-aided method of ~~identifying a ligand that binds to a protein~~selecting one or more conformations of a ligand likely to bind to a protein, said method comprising:

performing a pre-docking conformational search and generating multiple solution conformations of a ligand therefrom;

generating a binding site image of a protein, said binding site image comprising multiple hot spots;

matching hot spots of the binding site image to atoms in at least one conformation of the multiple solution conformations of the ligand to obtain at least one position of the ligand relative to the protein in a protein-ligand complex;

optimizing the at least one position of the ligand while allowing translation, orientation and rotatable bonds of the ligand to vary, and while holding the protein fixed;

calculating a score ~~based on the optimized position of the ligand that is predictive of the ligand's potential to bind to the protein~~indicative of a potential of a protein-ligand complex comprising the optimized position of the ligand; and

~~identifying said ligand as a ligand that binds to said protein if said score is above a threshold.~~

selecting one or more optimized ligand positions based on said score.

2. *(Previously Presented)* The method of claim 1, additionally comprising, after performing the pre-docking conformational search and generating multiple solution conformations, creating a database of the multiple solution conformations of the ligand and storing said three-dimensional database for subsequent use by said matching.

3. *(Previously Presented)* The method of claim 2, wherein said database of the multiple solution conformations of the ligand comprises a conformational database of a combinatorial library.